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Topical mitomycin C application post endoscopic removal of sinonasal inverted papilloma

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Abstract

Sinonasal inverted papilloma (IP), first described in 1854, is a benign epithelial lesion of the nasal cavity and paranasal sinuses, composed of well differentiated columnar or ciliated respiratory epithelium having variable squamous differentiation. The incidence of inverted papilloma has been reported as 0.2 to 0.7 cases per 100 000 population per year and comprise 0.5 to 4 % of primary nasal tumours . The most involved sites, in descending order, are: lateral nasal wall, ethmoid cells, maxillary sinus, and, less often, the frontal and sphenoid sinuses and nasal septum. Surgery is the first choice in the treatment of inverted papilloma. This study aimed to asses the effectiveness of mitomycin in reducing inverted papilloma's volume to undergo a less invasive surgical approach in order to reduce the risk of intra and post operative complications.1

Keywords

Sinonasal inverted papilloma (IP), endoscopic sinus surgery, mitomycin C, recurrence

Introduction

The World Health Organization (WHO) defines sinonasal inverted papilloma as a benign epithelial lesion composed of well differentiated columnar or ciliated respiratory epithelium having variable squamous differentiation. (1)

The WHO classifies IP as a subgroup of Schneiderian papillomas. The term inverted papilloma describes the histological appearance of the epithelium, i.e. inverting into the stroma, with a distinct and intact basement membrane that separates and defines the epithelial component from the underlying connective tissue stroma. (2)

The incidence of IP has been reported as 0.2 to 0.7 cases per 100 000 population per year (3) Inverted papillomas comprise 0.5 to 4 % of primary nasal tumours. (4) There is no site predilection, and bilateral cases are seen in 4.9 % of patients. The male to female ratio is 7:1 (5) with a higher prevalence in the Caucasian race. The peak age of presentation is in the fifth and the sixth decades (average age, 53 years);

The most common nasal sites involved by inverted papilloma, in order of descending prevalence, are: lateral nasal wall, ethmoid cells, maxillary sinus, and, less often, the frontal and sphenoid sinuses and nasal septum. (6) Inverted papilloma originating medially (i.e. from the septum or turbinates) comprises 34 %of reported cases; that originat-

ing laterally (i.e. from the sinuses and lateral nasal wall) makes up the rest (66 %).(7) The lateral nasal wall represents the most common site of origin, whereas paranasal sinuses are quite frequently found to be involved by extension. (8) However, isolated sphenoid involvement with inverted papilloma has been reported in a few cases . (8-9)

The main characteristics that distinguish it from other sinonasal tumors are: relative local aggression, high rates of recurrence , whether early or late, and possible association with carcinoma, diagnosed initially or at recurrence.

Etiology of IP remain mostly unknown. Certain hypotheses have been suggested, but causality has never been established for the suspected factors: smoking, allergy or certain occupational

exposures (10). Recurrence and carcinomatous potential have for many years suggested viral origin. An implication of Epstein–Barr Virus (EBV) has been studied, but inconclusively (11). For more than 30 years, human papilloma virus (HPV) has been suspected of playing a major role in the pathophysiology of IP, but the literature data remain contradictory (12) Clinical nonspecific symptoms of IP may include unilateral occlusion, rhinorrhea, sinus infection, and hyposmia/anosmia. Such primary manifestations may be accompanied by headaches and facial pain/pressure, lacrimation, or impaired vision (13) Endoscopically, the lesion appears as a grayish polypoid mass with a multinodular surface.(14) The treatment of choice is surgical; a purely endoscopic endonasal approach or combined endoscopic and external approach has now become the gold standard for many authors.(15) Chemotherapy and/or radiation therapy may follow surgery in case of malignant transformation; many authors have suggested that radiotherapy could be used for patients whose tumor has not been completely resected or in case of multiple recurrences.(16)

Mitomycin is derived from Streptomyces caespitosus and has antineoplastic activity similar to that of the alkylating agents. Mitomycin selectively inhibits the synthesis of DNA by causing cross-linking, degrades preformed DNA, and causes nuclear lysis and formation of giant cells. At high concentrations, cellular RNA and protein synthesis may also be suppressed. Mitomycin is cell cycle phase-nonspecific, although it has its maximum effect in late Gand early S-phases. It is used intravenously to treat uppergastro-intestinal cancers; however its most common usage is topically. Both human and animal applications confirm the safety of topical use of mitomycin-C (17,18) It has many topical usages by otolaryngologist in endoscopic sinus surgery, (19) choanal atresia,(20) laryngeal,(21) and tracheal surgery(22) to minimize or even prevent post-operative synechia and stenosis.

The aim of this study was to assess the effectiveness of mitomycin in reducing the size of IP recurrence after endoscopic endonasal approach.

Materials and methods

In January 2020 a 52 years old female, without comorbidities, underwent to ent examination for sinonasal symptoms: unilateral nasal obstruction, anterior and/or posterior rhinorrhea and hyposmia . Clinical examination by endoscopic exploration found, in the left nasal cavity, a reddish-gray lobulated tumor, more firm than an inflammatory polyp.

The patient underwent a CT scan and a MRI as a complement to CT.

Subsequently, endoscopic biopsy was performed with the histogical diagnosis of pT3 inverted papilloma (according to Krouse's classification).

According to literature data, a pT3 inverted papilloma (according to Krouse's classification) extended up to the anterior wall of the maxillary sinus would require extensively demolitive surgical treatment capable of widely exposing the maxillary sinus up to its anterior wall. In these cases, a type III median maxillectomy (also called "Sturmann-Canfield" surgery in which the maxillectomy is enlarged anteriorly to include the nasolacrimal duct up to the exposure of the piriform notch) is generally proposed.

This type of surgical intervention was proposed to the patient and the risks and complications related to surgery was explained: surgical approach was refused.

After an extensive informative interview with the patient and after authorization of the local ethics committee, it was decided to proceed with local dressings with 5% Mitomycin once a month for 6 months.

Therefore, starting from October 2020, the patient was subjected to local dressings under endoscopic guidance in local anesthesia: during the dressings, after local anesthesia, the edged gauze was placed at the level of the left maxillary cavity. Subsequently it was soaked with 5% Mitomycin. The dressing was left in place for 30 minutes and then removed.

This dressing was repeated in November 2020, December 2020 and January 2021. At the endoscopic follow-up in January 2021 there was a clear reduction in the hyperplastic area reported in October 2020. Therefore, in agreement with the patient, it was decided to practice two other dressings (February 2021 and March 2021) and to evaluate, subsequently, endoscopic revision surgery which, in consideration of the volumetric reduction of the lesion, will certainly be less invasive than expected at the beginning.

In our case, following the topical chemotherapy treatment with mitomycin, we obtained a complete reabsorption of the PI at the level of the anterior wall and the zygomatic process.

Therefore we decided to plan a type II median maxillectomy with preservation of the nasolacromal duct. In order to dominate the anterior wall of the left maxillary sinus more easily, we enlarged the maxillectomy anteriorly keeping ourselves under the Hasner valve, preserving the nasolacrimal duct: this allowed us to perform an easy maxillary sinusoscopy also at the level of the anterior wall thanks to the use of a 70° optic.

Contrary to what appeared from the radiological investigation performed before the treatment with mitomycin, we found an absence of involvement of the anterior maxillary wall by the IP. Therefore, having observed a PI limited to the posterior and medial walls, we decided not to perform a type III maxillectomy. Furthermore, since the neoformation extended to the anterior third of the middle meatus, we performed a subtotal resection of the first portion of the middle turbinate, a total uncinectomy with opening of the frontal pre-chambers and the opening of the bulla ethmoidalis. We performed opening of the second portion of the middle turbinate and subsequent posterior ethmoidectomy (surgical time 120 minutes) We also greatly reduced the risk of post-operative complications compared to a type III maxillectomy

The postoperative course was regular and uneventful. The patient was subjected to periodic (monthly) checks for about 6 months. During the checks, nasal endoscopy under local anesthesia was performed. No signs of disease recurrence were found during the controls.

Discussion

The main treatment of IP is surgery, and the cornerstone of successful surgery is the radical exeresis of the lesion.

However there is a high risk of recurrence especially for lesions located in areas that are difficult to control with the surgical endoscopic approach.

In the current study we used the MMC application to decrease the the volume of the lesion and minimal morbidly effect of transnasal endoscopic approach.

Mitomycin-C (MMC) has also many topical usages in otolaryngology. It was used safely to reduce nasal synechiae and stenosis after endoscopic sinus surgery,(10) and choanal atresia (11).

The etiopathogenesis of the IP is still not well understood but this effect of MMC in minimizing IP volume could be attributed to that the MMC is a chemotherapeutic agent that inhibits the DNA synthesis and so inhibits cell migration and mitosis decreasing the rate of cell proliferation. MMC was applied easily and safely without any added risk to the patients; no granulations, crusts, infection, bleeding was reported in the clinical case with its usage.

The technique proved to be safe, reliable, easily applicable and effective.

In particular, we demonstrated how the use of mitomycin was useful in order to reduce the volume of the lesion and make the following endoscopic surgical treatment less invasive.

Conclusion

Topical MMC application in nasosinusal inverted papilloma, is safe and effective in reducing the volume of the lesion and planning less invasive endoscopic surgical treatments in order to reduce intra and post-operative complications.

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Author contributions

MC, EP performed manuscript preparation; EP, EC performed final edits and revisions; LB, AM, CB read and approved the submitted version.

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